

Practice guideline update summary: Pharmacologic treatment for pediatric migraine prevention

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society

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Neurology® 2019;93:500-509. doi:10.1212/WNL.00000000000008105

Abstract

Objective

To provide updated evidence-based recommendations for migraine prevention using pharmacologic treatment with or without cognitive behavioral therapy in the pediatric population.

Methods

The authors systematically reviewed literature from January 2003 to August 2017 and developed practice recommendations using the American Academy of Neurology 2011 process, as amended.

Results

Fifteen Class I–III studies on migraine prevention in children and adolescents met inclusion criteria. There is insufficient evidence to determine if children and adolescents receiving divalproex, onabotulinumtoxinA, amitriptyline, nimodipine, or flunarizine are more or less likely than those receiving placebo to have a reduction in headache frequency. Children with migraine receiving propranolol are possibly more likely than those receiving placebo to have an at least 50% reduction in headache frequency. Children and adolescents receiving topiramate and cinnarizine are probably more likely than those receiving placebo to have a decrease in headache frequency. Children with migraine receiving amitriptyline plus cognitive behavioral therapy are more likely than those receiving amitriptyline plus headache education to have a reduction in headache frequency.

Recommendations

The majority of randomized controlled trials studying the efficacy of preventive medications for pediatric migraine fail to demonstrate superiority to placebo. Recommendations for the prevention of migraine in children include counseling on lifestyle and behavioral factors that influence headache frequency and assessment and management of comorbid disorders associated with headache persistence. Clinicians should engage in shared decision-making with patients and caregivers regarding the use of preventive treatments for migraine, including discussion of the limitations in the evidence to support pharmacologic treatments.



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Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Approved by the American Academy of Neurology (AAN) Guideline Development, Dissemination, and Implementation Subcommittee on October 20, 2018; by the AAN Practice Committee on March 29, 2019; by the AAN Institute Board of Directors on April 10, 2019; and by the American Headache Society Board of Directors on May 1, 2019.

This practice guideline was endorsed by the Child Neurology Society on February 9, 2019; and the American Academy of Pediatrics on April 8, 2019.

Table Outcomes and confidence in evidence

| Outcome | High confidence (more likely than placebo) | Moderate confidence (probably more likely than placebo) | Low confidence (possibly more likely than placebo) | Moderate confidence (probably no more likely than placebo) | Low confidence (possibly no more likely than placebo) | Very low confidence (insufficient evidence) |
|--|---|--|---|--|---|--|
| Decreased frequency of migraine or headache days | Amitriptyline (1 mg/kg/d) combined with CBT | Topiramate (100 mg/d or 2–3 mg/kg/d) Cinnarizine (1.5 mg/kg/d if <30 kg or 50 mg/d if >30 kg) | | | | DVPX ER (250 mg/d, 500 mg/d, or 1,000 mg/d) Amitriptyline (1 mg/kg/d) Flunarizine (5 mg/d) Nimodipine (10–20 mg, 3 times a day) OnabotulinumtoxinA (74 U IM or 155 U IM) |
| Decreased headache severity | | Cinnarizine (1.5 mg/kg/d if <30 kg or 50 mg/d if >30 kg) | | | | |
| At least a 50% reduction in headache frequency | Amitriptyline (1 mg/kg/d) combined with CBT | | Propranolol (20–40 mg, 3 times a day) Cinnarizine (1.5 mg/kg/d if <30 kg or 50 mg/d if >30 kg) | | | Topiramate (100 mg/d or 2–3 mg/kg/d) DVPX ER (250 mg/d, 500 mg/d, or 1,000 mg/d) Amitriptyline (1 mg/kg/d) OnabotulinumtoxinA (74 U IM or 155 U IM) |
| Decreased migraine-related disability | | Amitriptyline (1 mg/kg/d) combined with CBT | | | Topiramate (100 mg/d or 2–3 mg/kg/d) | Amitriptyline (1 mg/kg/d) |

Abbreviations: CBT = cognitive behavioral therapy; DVPX ER = extended-release divalproex sodium.

0.43 [95% CI 0.09–0.77]; moderate confidence in the evidence, 1 Class I study²⁹).

Practice recommendations

Counseling and education for children and adolescents with migraine and their families

Recommendation 1 rationale

Individuals with a family history of migraine are at higher risk of developing migraine, and female sex is a risk factor of migraine that persists into adulthood.³⁰ Disease prevention is the cornerstone of medical care. Migraine has multiple behavioral factors that influence headache frequency. Recurrent headache in adolescents is associated with being overweight, caffeine and alcohol use, lack of physical activity, poor sleep habits, and tobacco exposure.³¹ Depression is associated with higher headache disability in adolescents.³² Weight loss can contribute to headache reduction in children who are overweight.³³ Identification and avoidance of factors that contribute to headache risk can reduce migraine frequency.

Statement 1a

Clinicians should counsel patients and families that lifestyle and behavioral factors may influence headache frequency (Level B).

Statement 1b

Clinicians should educate patients and families to identify and modify migraine contributors that are potentially modifiable (Level B).

Recommendation 2 rationale

In adults with migraine, headache on more than 6 days in a month is a risk factor for progression to chronic migraine, with medication overuse contributing to this progression.³⁴ Taking triptans, ergotamines, opioids, and combination analgesics on more than 9 days in a month or taking over-the-counter simple analgesics on more than 14 days in a month can lead to medication overuse headache. (There is no evidence to support the use of opioids in children with migraine. Opioids are included in this rationale to be consistent with the International Classification of Headache Disorders³⁵ regarding medication overuse.) It has been suggested that clinicians consider preventive treatments in these populations.³⁶ Although there are no data on this topic in pediatric populations, it is hypothesized that similar relationships between frequent headache, medication overuse, and progression to chronic migraine may occur in children. In clinical trials of pediatric migraine prevention, inclusion criteria for headache frequency were variable and included a minimum of 4 headache days per month with no maximum and 3–4 migraine attacks per month for at least 3

Practice guideline update summary: Acute treatment of migraine in children and adolescents

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Neurology® 2019;93:487-499. doi:10.1212/WNL.0000000000008095

Abstract

Objective

To provide evidence-based recommendations for the acute symptomatic treatment of children and adolescents with migraine.

Methods

We performed a systematic review of the literature and rated risk of bias of included studies according to the American Academy of Neurology classification of evidence criteria. A multidisciplinary panel developed practice recommendations, integrating findings from the systematic review and following an Institute of Medicine-compliant process to ensure transparency and patient engagement. Recommendations were supported by structured rationales, integrating evidence from the systematic review, related evidence, principles of care, and inferences from evidence.

Results

There is evidence to support the efficacy of the use of ibuprofen, acetaminophen (in children and adolescents), and triptans (mainly in adolescents) for the relief of migraine pain, although confidence in the evidence varies between agents. There is high confidence that adolescents receiving oral sumatriptan/naproxen and zolmitriptan nasal spray are more likely to be headache-free at 2 hours than those receiving placebo. No acute treatments were effective for migraine-related nausea or vomiting; some triptans were effective for migraine-related phonophobia and photophobia.

Recommendations

Recommendations for the treatment of acute migraine in children and adolescents focus on the importance of early treatment, choosing the route of administration best suited to the characteristics of the individual migraine attack, and providing counseling on lifestyle factors that can exacerbate migraine, including trigger avoidance and medication overuse.



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Outcome: Pain response at 30 minutes

Low confidence in the evidence

Adolescents receiving sumatriptan nasal spray (NS) 20 mg are possibly more likely than those receiving placebo to have a headache pain response at 30 minutes (relative risk [RR] 1.27; 95% confidence interval [CI], 1.01–1.60; 1 Class I⁴ study).

Very low confidence in the evidence

There is insufficient evidence to determine whether adolescents receiving sumatriptan NS 5 mg are more or less likely than those receiving placebo to have a headache pain response at 30 minutes (RR 1.03; 95% CI 0.80–1.32; 1 Class I⁴ study).

There is insufficient evidence to determine whether children and adolescents receiving the following treatments are more or less likely than those receiving placebo to have a headache pain response at 30 minutes:

- Sumatriptan oral tablet (OT) 25 mg (RR 0.35; 95% CI 0.03–4.14; 1 Class I⁵ study)
- Sumatriptan OT 50 mg (RR 2.27; 95% CI 0.58–8.90; 1 Class I⁵ study)

Outcome: Pain response at 1 hour

Moderate confidence in the evidence

Adolescents receiving sumatriptan NS 5 mg are probably no more likely than those receiving placebo to have a headache pain response at 1 hour (RR 1.05; 95% CI 0.91–1.21; 1 Class I⁴ and 1 Class II⁶ study).

Low confidence in the evidence

Children and adolescents receiving the following treatments are possibly more likely than those receiving placebo to have a headache pain response at 1 hour:

- Sumatriptan NS 10 mg (RR 1.55; 95% CI 1.08–2.23; 2 Class II studies^{6,7})

Table 1 Pain outcomes and confidence in evidence

| Outcome | High confidence (more likely than placebo) | Moderate confidence (probably more likely than placebo) | Low confidence (possibly more likely than placebo) | Moderate confidence (probably no more likely than placebo) | Low confidence (possibly no more likely than placebo) | Very low confidence (insufficient evidence) |
|-----------------------------|--|---|--|--|---|--|
| Pain response at 30 minutes | | | Sumatriptan NS 20 mg | | | Sumatriptan NS 5 mg Sumatriptan OT 25 mg Sumatriptan OT 50 mg |
| Pain response at 1 hour | | | Zolmitriptan NS 5 mg Sumatriptan NS 10 mg Sumatriptan NS 20 mg | Sumatriptan NS 5 mg | | Sumatriptan OT 25 mg Sumatriptan OT 50 mg |
| Pain response at 2 hours | | | Ibuprofen OS 7.5–10 mg/kg Acetaminophen OS 15 mg/kg Almotriptan OT 6.25 mg Almotriptan OT 12.5 mg Sumatriptan NS 20 mg Zolmitriptan NS 5 mg | Rizatriptan ODT 5 or 10 mg | Eletriptan OT 40 mg | Almotriptan OT 25 mg Sumatriptan NS 5 mg Sumatriptan NS 10 mg Sumatriptan OT 25 mg Sumatriptan OT 50 mg |
| Pain-free at 1 hour | | Zolmitriptan NS 5 mg | | | | |
| Pain-free at 2 hours | Sumatriptan naproxen OT 10/60 mg Sumatriptan/naproxen OT 30/180 mg Sumatriptan/naproxen OT 85/500 mg Zolmitriptan NS 5 mg | Ibuprofen OS 7.5–10 mg/kg Sumatriptan NS 20 mg | Rizatriptan ODT 5 or 10 mg | | Almotriptan OT 12.5 mg | Acetaminophen OS 15 mg/kg Almotriptan OT 6.25 mg Almotriptan OT 25 mg Eletriptan OT 40 mg Sumatriptan OT 25 mg Sumatriptan OT 50 mg |

Abbreviations: NS = nasal spray; ODT = oral disintegrating tablet; OS = oral solution; OT = oral tablet.

Table 2 Associated symptom outcomes and confidence in evidence

| Outcome | High confidence (more likely than placebo) | Moderate confidence (probably more likely than placebo) | Low confidence (possibly more likely than placebo) | Moderate confidence (probably no more likely than placebo) | Low confidence (possibly no more likely than placebo) | Very low confidence (insufficient evidence) |
|-------------------------------------|---|---|--|--|--|--|
| Relief of nausea at 2 hours | | | | Sumatriptan NS 5 mg Sumatriptan NS 20 mg Sumatriptan/ naproxen OT 85/500 mg | Eletriptan OT 40 mg | Ibuprofen OS 7.5–10 mg/kg Sumatriptan NS 10 mg Sumatriptan/ naproxen OT 10/60 mg Sumatriptan/ naproxen OT 30/180 mg Rizatriptan ODT 5 or 10 mg |
| Relief of vomiting at 2 hours | | | | Sumatriptan NS 5 mg Sumatriptan NS 20 mg | Sumatriptan NS 10 mg Rizatriptan ODT 5 or 10 mg | |
| Relief of photophobia at 30 minutes | | Zolmitriptan NS 5 mg | | | | |
| Relief of photophobia at 2 hours | | Sumatriptan/ naproxen OT 10/60 mg Sumatriptan/ naproxen OT 85/500 mg | Zolmitriptan NS 5 mg | | Eletriptan OT 40 mg | Sumatriptan NS 10 mg Sumatriptan/ naproxen OT 30/180 mg Rizatriptan ODT 5 or 10 mg |
| Relief of phonophobia at 30 minutes | | Zolmitriptan NS 5 mg | | | | |
| Relief of phonophobia at 2 hours | | Sumatriptan/ naproxen OT 10/60 mg Sumatriptan/ naproxen OT 85/500 mg | Sumatriptan NS 5 mg Sumatriptan NS 20 mg Sumatriptan/ naproxen OT 30/180 mg | Rizatriptan ODT 5 or 10 mg | Eletriptan OT 40 mg | Sumatriptan NS 10 mg Zolmitriptan NS 5 mg |

Abbreviations: NS = nasal spray; ODT = oral disintegrating tablet; OS = oral solution; OT = oral tablet.

- Sumatriptan NS 20 mg (RR 1.27; 95% CI 1.09–1.49; 1 Class I⁴ and 2 Class II studies^{6,7})

Adolescents receiving zolmitriptan NS 5 mg are possibly more likely than those receiving placebo to have a headache pain response at 1 hour (RR 1.34; 95% CI 1.05–1.71; 1 Class II study⁸).

Very low confidence in the evidence

There is insufficient evidence to determine whether children and adolescents receiving the following treatments are more or less likely than those receiving placebo to have a headache pain response at 1 hour:

- Sumatriptan OT 25 mg (RR 0.49; 95% CI 0.16–1.48; 1 Class I study⁵)
- Sumatriptan OT 50 mg (RR 0.39; 95% CI 0.13–1.19; 1 Class I study⁵)

Outcome: Pain response at 2 hours

Moderate confidence in the evidence

Children and adolescents receiving 5 or 10 mg of rizatriptan oral disintegrating tablets (ODT) are probably no more likely than those receiving placebo to have a headache pain response at 2 hours (RR 1.07; 95% CI 0.97–1.17; 3 Class II studies^{9–11}).

Low confidence in the evidence

Children and adolescents receiving the following treatments are possibly more likely than those receiving placebo to have a headache pain response at 2 hours:

- Ibuprofen oral solution (OS) 7.5–10 mg/kg (RR 1.54; 95% CI 1.18–2.01; 1 Class II¹² and 1 Class III¹³ study)
- Acetaminophen OS 15 mg/kg (RR 1.46; 95% CI 1.02–2.09; 1 Class II study¹²)
- Sumatriptan NS 20 mg (RR 1.32; 95% CI 1.04–1.68; 1 Class I⁴ and 2 Class II^{6,7} studies)

Table 3 Confidence in evidence by drug and outcome

| | Pain response at 30 minutes | Pain response at 1 hour | Pain response at 2 hours | Pain-free at 1 hour | Pain-free at 2 hours | Relief of nausea at 2 hours | Relief of vomiting at 2 hours | Relief of photophobia at 2 hours | Relief of phonophobia at 2 hours |
|--|-----------------------------|--|--|---------------------|---|--|--|---|--|
| Ibuprofen OS 7.5–10 mg/kg | | | Low | | Moderate | Very low | | | |
| Acetaminophen OS 15 mg/kg | | | Low | | Very low | | | | |
| Sumatriptan OT 25 mg | Very low | Very low | Very low | | Very low | | | | |
| Sumatriptan OT 50 mg | Very low | Very low | Very low | | Very low | | | | |
| Sumatriptan NS 5 mg | Very low | Moderate: probably no more likely than placebo | Very low | | | Moderate: probably no more likely than placebo | Moderate: probably no more likely than placebo | Very low | Low |
| Sumatriptan NS 10 mg | | Low | Very low | | | Very low | Low: possibly no more likely than placebo | Very low | Very low |
| Sumatriptan NS 20 mg | Low | Low | Low | | Moderate | Moderate: probably no more likely than placebo | Moderate: probably no more likely than placebo | Very low | Low |
| Sumatriptan/naproxen OT 10/60 mg | | | | | High | Very low | | Moderate | Moderate |
| Sumatriptan/naproxen OT 30/180 mg | | | | | High | Very low | | Very low | Low |
| Sumatriptan/naproxen OT 85/500 mg | | | | | High | Moderate: probably no more likely than placebo | | Moderate | Moderate |
| Rizatriptan ODT 5 or 10 mg | | | Moderate: probably no more likely than placebo | | Low | Very low | Low: possibly no more likely than placebo | Very low | Moderate: probably no more likely than placebo |
| Eletriptan OT 40 mg | | | Low: possibly no more likely than placebo | | Very low | Low: possibly no more likely than placebo | | Low: possibly no more likely than placebo | Low: possibly no more likely than placebo |
| Zolmitriptan NS | | Low | Low | Moderate | High | | | Low | Very low |
| Almotriptan OT 6.25 mg | | | Low | | Very low | | | | |
| Almotriptan OT 12.5 mg | | | Low | | Low: possibly no more likely than placebo | | | | |
| Almotriptan OT 25 mg | | | Very low | | Very low | | | | |

Abbreviations: NS = nasal spray; ODT = oral disintegrating tablet; OS = oral solution; OT = oral tablet.